

a) contacting a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:5, or a cell expressing a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:5 with a test compound; and

b) determining whether the polypeptide binds to the test compound.

- a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay;
- c) detection of binding using an assay for NBS-1 or PYRIN-1-mediated signal transduction;
- d) detection of binding using an assay for proteolytic activity;
- e) detection of binding to a pyrin domain; and
- f) detection of binding to ASC.

4. A method for identifying a compound which modulates the activity of a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:5, the method comprising:

a) contacting the polypeptide with a test compound; and

b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

5. A method of treating a disorder associated with inappropriate apoptosis, the method comprising modulating the expression or activity of NBS-1 or PYRIN-1.

5 6. A method for identifying a candidate compound for modulating the binding of PYRIN-1 to ASC, the method comprising:

a) measuring the binding of a first polypeptide comprising the pyrin domain of ASC to a second polypeptide comprising the pyrin domain of PYRIN-1 in the presence of a test compound; and

10 b) comparing the binding of the first polypeptide to the second polypeptide measured in step (a) to the binding of the first polypeptide to the second polypeptide in the absence of the test compound,

15 wherein altered binding of the first polypeptide to the second polypeptide in the presence of the test compound compared the binding in the absence of the test compound indicates that the test compound modulates the binding of PYRIN-1 to ASC.

7. A method for identifying a candidate compound for modulating the ASC-mediated activation of NF-kB, the method comprising:

20 a) measuring the binding of a first polypeptide comprising the pyrin domain of ASC to a second polypeptide comprising the pyrin domain of PYRIN-1 in the presence of a test compound; and

b) comparing the binding of the first polypeptide to the second polypeptide measured in step (a) to the binding of the first polypeptide to the second polypeptide in the absence of the test compound,

25 wherein altered binding of the first polypeptide to the second polypeptide in the presence of the test compound compared the binding in the absence of the test compound indicates that the test compound is candidate compound for modulating the ASC-mediated activation of NF-kB.

8. A method for identifying an modulator of NF-kB activity, the method comprising:

- a) providing a cell expressing recombinant ASC and recombinant PYRIN-1;
- b) exposing the cell to a test compound; and
- c) measuring the NK-kB activity of the cell in the presence of the test compound

wherein altered activation in the presence of the test compound compared to the absence of the test compound indicates that the compound is a modulator of NF-kB activity.

9. A method for identifying a candidate compound for modulating the ASC-mediated activation of NF-kB, the method comprising:

- a) measuring the binding of a test compound to the LRR domain of PYRIN-1; and
- b) determining that the test compound is a candidate compound for modulating the ASC-mediated activation of NF-kB when the test compound binds to the LRR domain of PYRIN-1.

10. A method for identifying a candidate compound for modulating the ASC-mediated activation of NF-kB, the method comprising:

- a) measuring the binding of a test compound to the LRR domain of PYRIN-1; and
- b) identifying the test compound as an LRR domain binding compound when the test compound binds to the LRR domain of PYRIN-1;

- c) measuring the activation of NF-kB in a cell expressing ASC and PYRIN-1 in the presence and absence of the LRR domain binding compound,

wherein the LRR domain binding compound is a candidate compound for modulating the ASC-mediated activation of NF-kB if the activation of NF-kB in the presence of the LRR domain binding compound is greater than in the absence of the LRR domain binding compound.

11. A method for identifying a candidate modulator of PYRIN-1, the method comprising:

- 5

10

14.

15

20

17.

25

- a)

b) measuring the binding of the nucleotide to the NBS domain in the presence of the test compound;

c) identifying a test compound that reduces the binding of the nucleotide to the NBS domain; and

5 d) measuring the binding of a test compound that reduces the binding of the nucleotide to the NBS domain of PYRIN-1 to an NBS domain of a protein other than PYRIN-1;

10 wherein the test compound is a candidate modulator of PYRIN-1 if it reduces the binding of the nucleotide to the NBS domain of PYRIN-1 and does not substantially reduce the binding of the nucleotide of the NBS domain of a protein other than PYRIN-1.

18 19. The method of claim 18 wherein in the NBS of a protein other than PYRIN-1 is the NBS domain of a protein selected from the group consisting of: NBS-1, CARD-12, and CARD-4.

15 19 20. A method for identifying a candidate modulator of PYRIN-1, the method comprising:

20 a) contacting a purified polypeptide comprising the NBS domain of PYRIN-1 with a test compound in the presence of a nucleotide triphosphate that binds to the NBS domain in the absence of the test compound;

b) measuring the hydrolysis of the nucleotide triphosphate in the presence of the test compound; and

c) identifying the test compound is a candidate modulator of PYRIN-1 if the test compound reduces the hydrolysis of the nucleotide triphosphate.

25 21. A method for modulating ASC activity in a patient, the method comprising administering a compound that alters the activity of PYRIN-1.

22. 22. A method for modulating NF-kB activity in a patient, the method comprising administering a compound that alters the activity of PYRIN-1.

30

23. A method for treating an inflammatory disorder in a patient, the method comprising administering a compound that alters the activity of PYRIN-1.

24. A method for identifying a candidate compound for treating an inflammatory disorder, the method comprising:

a) measuring the binding of a first polypeptide comprising the pyrin domain of ASC to a second polypeptide comprising the pyrin domain of PYRIN-1 in the presence of a test compound; and

b) comparing the binding of the first polypeptide to the second polypeptide measured in step (a) to the binding of the first polypeptide to the second polypeptide in the absence of the test compound,

wherein altered binding of the first polypeptide to the second polypeptide in the presence of the test compound compared the binding in the absence of the test compound indicates that the test compound is a candidate compound for treating an inflammatory disorder.

25. A method for identifying a candidate compound for treating an inflammatory disorder, the method comprising:

a) measuring the binding of a first polypeptide comprising the pyrin domain of ASC to a second polypeptide comprising the pyrin domain of PYRIN-1 in the presence of a test compound; and

b) comparing the binding of the first polypeptide to the second polypeptide measured in step (a) to the binding of the first polypeptide to the second polypeptide in the absence of the test compound,

wherein altered binding of the first polypeptide to the second polypeptide in the presence of the test compound compared the binding in the absence of the test compound indicates that the test compound is candidate compound treating an inflammatory disorder.

2.5
26. A method for identifying a candidate compound for treating an inflammatory disorder, the method comprising:

- a) providing a cell expressing recombinant ASC and recombinant PYRIN-1;
- b) exposing the cell to a test compound; and
- 5 c) measuring the NK-kB activity of the cell in the presence of the test compound wherein altered activation in the presence of the test compound compared to the absence of the test compound indicates that the compound is a candidate compound for treating an inflammatory disorder.

10 27. 4 A method for identifying a candidate compound for treating an inflammatory, the method comprising:

- a) measuring the binding of a test compound to the LRR domain of PYRIN-1; and
- b) determining that the test compound is a candidate compound for candidate compound for treating an inflammatory when the test compound binds to the LRR domain of PYRIN-1.

15 28. 21 A method for identifying candidate compound for treating an inflammatory disorder, the method comprising:

- a) measuring the binding of a test compound to the LRR domain of PYRIN-1; and
- b) identifying the test compound as an LRR domain binding compound when the test compound binds to the LRR domain of PYRIN-1;

20 c) measuring the activation of NF-kB in a cell expressing ASC and PYRIN-1 in the presence and absence of the LRR domain binding compound,

wherein the LRR domain binding compound is a candidate compound for treating an inflammatory disorder if the activation of NF-kB in the presence of the LRR domain binding compound is greater than in the absence of the LRR domain binding compound.

25 29. 26 A method for identifying candidate compound for treating an inflammatory disorder, the method comprising:

a) contacting a purified polypeptide comprising the NBS domain of PYRIN-1 with a test compound in the presence of a nucleotide that binds to the NBS domain in the absence of the test compound;

b) measuring the binding of the nucleotide to the NBS domain in the presence of the test compound; and

c) identifying the test compound as a candidate compound for treating an inflammatory disorder if the test compound reduces the binding of the nucleotide to the NBS domain.